STIC Search Report
Biotech-Chem Library

USPTO

STIC Database Tracking Number: 114157

TO: Ruth Davis **Location: REM-3D71** **Art Unit: 1651** **Thursday, February 12, 2004** **Case Serial Number: 09/284806**	**From: Alex Waclawiw** **Location: Biotech-Chem Library** **Rem 1A71** **Phone: 308-4491** **Alexandra.waclawiw@uspto.gov**

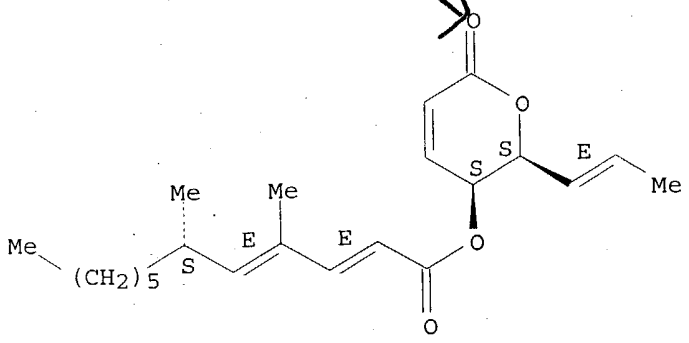
3E71

Search Notes

Examiner Davis,

This is the structure for the compound that you specified. The inventor named it differently than CAS. Ignore the stereochemistry since a basic structure search includes all stereochemistry. See references for the structure hits.
If you have any questions please feel free to contact me.

Alexandra Waclawiw



sira
Search and Information Resources Administration

114157

Request a Prior Art Search

Search requests relating to **published applications, patent families, and litigation** may be submitted by filling out this form and clicking on "Send."

For all other search requests, fill out the form, print, and submit the printout with any attachments to the STIC facility serving your Technology Center.

Tech Center:

(•) TC 1600 ( ) TC 1700 ( ) TC 2100 ( ) TC 2600
( ) TC 2800 ( ) TC 3600 ( ) TC 3700 ( ) Other

Enter your Contact Information below:

Name: Ruth Davis
Employee Number: 78220 Phone: 571-272-0915
Art Unit or Office: 1651 Building & Room Number: REM 3D71

3E71

RECEIVED
FEB 11 2001
(STIC)

Enter the case serial number (Required): 09/284,806
If not related to a patent application, please enter NA here.

Class / Subclass(es)

Earliest Priority Filing Date: 10/21/97

Format preferred for results:
[x] *Paper* [ ] *Diskette* [x] *E-mail*

Provide detailed information on your search topic:

- In your own words, describe in detail the concepts or subjects you want us to search.
- Include synonyms, keywords, and acronyms. Define terms that have special meanings.
- *For Chemical Structure Searches Only*
  Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers
- *For Sequence Searches Only*
  Include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.
- *For Foreign Patent Family Searches Only*
  Include the country name and patent number.
- Provide examples or give us relevant citations, authors, etc., if known.
- FAX or send the **abstract, pertinent claims** (not all of the claims), **drawings, or chemical structures** to your EIC or branch library.

pp. 25 - 50

Enter your Search Topic Information below:

Please search the structures of claims 1 and 3.

specifically:

3-((5S,6S)-5,6-dihydro-5-((6S)-4,6-dimethydodeca-2E,4E-dienoyl)-2H-pyran-2-on-6-yl)-prop-2E-enoic acid

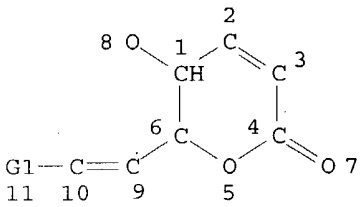
Special Instructions and Other Comments:
(For fastest service, let us know the best times to contact you, in case the searcher needs further clarification on your search.)

Press ALT + F, then P to print this screen for your own information.

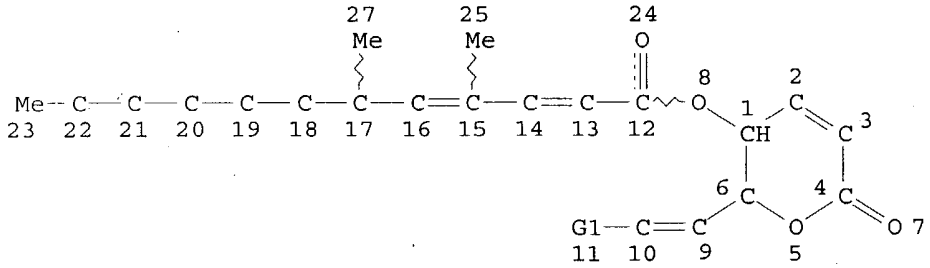
SEND RESET

```
=> d his

     (FILE 'REGISTRY' ENTERED AT 12:15:04 ON 12 FEB 2004)
               DEL HIS Y

     FILE 'REGISTRY' ENTERED AT 12:16:43 ON 12 FEB 2004
               ACT DAVISCLM1/A
               ---------
L1             STR
L2   (       58)SEA FILE=REGISTRY SSS FUL L1
L3             STR
L4            6 SEA FILE=REGISTRY SUB=L2 SSS FUL L3
               ---------
               ACT FORMII/A
               ---------
L5             STR
L6   (       58)SEA FILE=REGISTRY SSS FUL L5
L7   (     4085)SEA FILE=REGISTRY ABB=ON  PLU=ON  C8H10O3
L8   (        4)SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 AND L6
L9   (      363)SEA FILE=REGISTRY ABB=ON  PLU=ON  C8H8O5
L10  (        1)SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND L6
L11           5 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 OR L10
               ---------
               ACT FORMIIIA/A
               ---------
L12  (     3569)SEA FILE=REGISTRY ABB=ON  PLU=ON  C14H24O2
L13  (       12)SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 AND 2 4 DODECADIENOIC
L14           3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L13 AND 4 6 DIMETHYL
               ---------
               SELECT RN L14 1-3
               SELECT RN L16 1-3
               SET SMARTSELECT ON
L15        SEL L11 1- RN :       5 TERMS
               SET SMARTSELECT OFF
L16           0 S L15/CRN
               SET SMARTSELECT ON
L17        SEL L14 1- RN :       3 TERMS
               SET SMARTSELECT OFF
L18           0 S L17/CRN

     FILE 'CAPLUS' ENTERED AT 12:25:57 ON 12 FEB 2004
L19           6 S L4
L20           2 S L11 AND L14
```

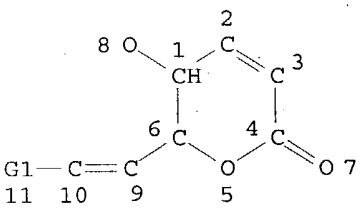
```
=> fil reg
FILE 'REGISTRY' ENTERED AT 12:28:49 ON 12 FEB 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   11 FEB 2004  HIGHEST RN 649538-27-2
DICTIONARY FILE UPDATES:  11 FEB 2004  HIGHEST RN 649538-27-2

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d que stat l4
L1                STR
```




```
VAR G1=CO2H/ME
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  11

STEREO ATTRIBUTES: NONE
L2  (        58)SEA FILE=REGISTRY SSS FUL L1
L3                STR
```



```
VAR G1=CO2H/ME
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  26

STEREO ATTRIBUTES: NONE
L4            6 SEA FILE=REGISTRY SUB=L2 SSS FUL L3

100.0% PROCESSED      6 ITERATIONS                                 6 ANSWERS
SEARCH TIME: 00.00.01


=> d que l11
L5                 STR
```




```
VAR G1=CO2H/ME
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  11

STEREO ATTRIBUTES: NONE
L6   (        58)SEA FILE=REGISTRY SSS FUL L5
L7   (      4085)SEA FILE=REGISTRY ABB=ON  PLU=ON  C8H10O3
L8   (         4)SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 AND L6
L9   (       363)SEA FILE=REGISTRY ABB=ON  PLU=ON  C8H8O5
L10  (         1)SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND L6
L11             5 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 OR L10


=> d que stat l14
L12  (      3569)SEA FILE=REGISTRY ABB=ON  PLU=ON  C14H24O2
L13  (        12)SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 AND 2 4 DODECADIENOIC
L14             3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L13 AND 4 6 DIMETHYL


=> d his l15-l18

     (FILE 'REGISTRY' ENTERED AT 12:16:43 ON 12 FEB 2004)
               ---------
                SELECT RN L14 1-3
                SELECT RN L16 1-3
                SET SMARTSELECT ON
L15          SEL L11 1- RN :       5 TERMS
```

```
                SET SMARTSELECT OFF
L16           0 S L15/CRN
                SET SMARTSELECT ON
L17         SEL L14 1- RN :       3 TERMS
                SET SMARTSELECT OFF
L18           0 S L17/CRN

=> fil caplus
FILE 'CAPLUS' ENTERED AT 12:30:01 ON 12 FEB 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 12 Feb 2004  VOL 140 ISS 7
FILE LAST UPDATED: 11 Feb 2004  (20040211/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que nos l19
L1              STR
L2  (       58)SEA FILE=REGISTRY SSS FUL L1
L3              STR
L4            6 SEA FILE=REGISTRY SUB=L2 SSS FUL L3
L19           6 SEA FILE=CAPLUS ABB=ON  PLU=ON  L4


=> d que nos l20
L5              STR
L6  (        58)SEA FILE=REGISTRY SSS FUL L5
L7  (      4085)SEA FILE=REGISTRY ABB=ON  PLU=ON  C8H10O3
L8  (         4)SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 AND L6
L9  (       363)SEA FILE=REGISTRY ABB=ON  PLU=ON  C8H8O5
L10 (         1)SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND L6
L11           5 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 OR L10
L12 (      3569)SEA FILE=REGISTRY ABB=ON  PLU=ON  C14H24O2
L13 (        12)SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 AND 2 4 DODECADIENOIC
L14           3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L13 AND 4 6 DIMETHYL
L20           2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L11 AND L14


=> d .ca hitstr l19 1-6;d .ca hitstr l20 1-2

L19  ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2002:340575  CAPLUS
DOCUMENT NUMBER:          137:108320
TITLE:                    Identifying protein kinase inhibitors using an assay
```

based on inhibition of aerial hyphae formation in Streptomyces

AUTHOR(S): Waters, Barbara; Saxena, Geeta; Wanggui, Yangsheng; Kau, David; Wrigley, Stephen; Stokes, Richard; Davies, Julian

CORPORATE SOURCE: Cubist Pharmaceuticals, Inc., Vancouver, BC, V6T 1Z3, Can.

SOURCE: Journal of Antibiotics (2002), 55(4), 407-416
CODEN: JANTAJ; ISSN: 0021-8820

PUBLISHER: Japan Antibiotics Research Association

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have identified a strain of Streptomyces in which aerial hyphae formation appears to be especially sensitive to inhibition by protein kinase inhibitors. Using this assay, a number of bacterial cultures have been screened and novel inhibitors of eukaryotic protein kinases have been identified. Since M. tuberculosis possesses multiple eukaryotic-like protein kinase genes, we tested the active kinase inhibitors for the inhibition of mycobacterial growth and obtained several potent compds. This identifies a new biochem. class of antimycobacterial agents.

CC 16-1 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 9

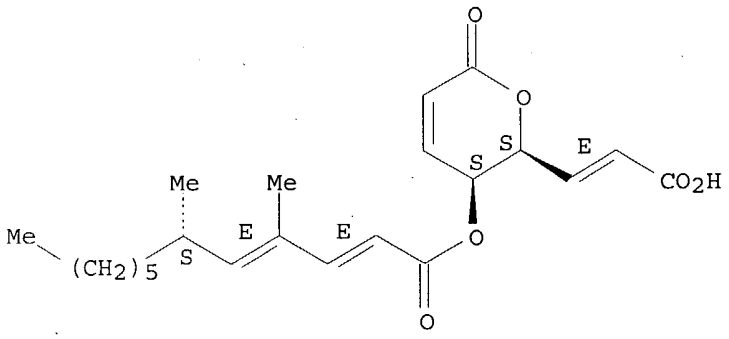
IT 446-72-0, Genistein 18791-21-4, Pyridomycin 24730-31-2, Surfactin 27127-62-4, Viscosin 71897-07-9, Ag-1295 131956-33-7, Depsidomycin 133550-30-8, Ag-490 153436-53-4, Ag-1478 169062-92-4, Cyclomarin a 192819-12-8, XR 587 **207220-91-5**, Xr-379 339320-58-0, Xr-774 343780-48-3, Xr-336 405149-80-6, Xr-543 405149-83-9, Xr-318 405150-05-2, Xr-665 405150-10-9, Xr-315 405150-11-0, Xr-475 405150-13-2, Xr-819
RL: BSU (Biological study, unclassified); BIOL (Biological study) (identifying protein kinase inhibitors using assay based on inhibition of aerial hyphae formation in Streptomyces)

IT **207220-91-5**, Xr-379
RL: BSU (Biological study, unclassified); BIOL (Biological study) (identifying protein kinase inhibitors using assay based on inhibition of aerial hyphae formation in Streptomyces)

RN 207220-91-5 CAPLUS

CN 2,4-Dodecadienoic acid, 4,6-dimethyl-, (2S,3S)-2-[(1E)-2-carboxyethenyl]-3,6-dihydro-6-oxo-2H-pyran-3-yl ester, (2E,4E,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:220383 CAPLUS
DOCUMENT NUMBER: 136:259921
TITLE: Antibacterial agents and methods of identification
INVENTOR(S): Davies, Julian E.; Waters, Barbara
PATENT ASSIGNEE(S): Cubist Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022138	A1	20020321	WO 2001-US28913	20010917
WO 2002022138	C2	20031106		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

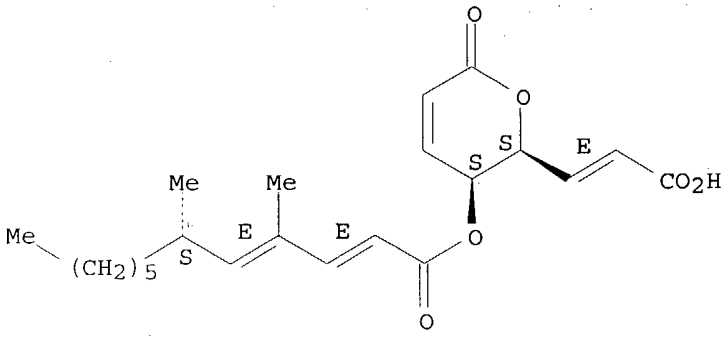
AU 2001096253	A5	20020326	AU 2001-96253	20010917
PRIORITY APPLN. INFO.:			US 2000-233004P P	20000915
			WO 2001-US28913 W	20010917

AB The present invention provides an assay based on Streptomyces species in which aerial hyphae formation and sporulation appear to be especially sensitive to inhibition by protein kinase inhibitors which are also antibacterial agents. Using this Streptomyces-based assay and a growth inhibitory assay, a number of bacterial cultures have been examined and several potential novel inhibitors of antimycobacterial agents have been identified. The antibacterial screening method of the invention comprises two step: (a) contacting a growing culture of Streptomyces griseus or Streptomyces 85E with a test compound for a time sufficient to allow the test compound to alter aerial mycelial development or sporulation, and (b) contacting mycobacterium cells with the test compound of step (a) for a time sufficient to allow the test compound to inhibit growth of the mycobacterium. Test compds. that tested pos. in both step (a) and step (b) are antibacterial compds. of the invention.

IC ICM A61K031-70
ICS A61K031-33; A61K035-00; C12Q001-48
CC 10-5 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 1
IT **207220-91-5**, XR 379
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(XR 379; antibacterial agents and methods of identification based on Streptomyces species and inhibition of Mycobacterium and purification from microbial cell culture supernatant)
IT **207220-91-5**, XR 379
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(XR 379; antibacterial agents and methods of identification based on Streptomyces species and inhibition of Mycobacterium and purification from microbial cell culture supernatant)
RN 207220-91-5 CAPLUS

CN 2,4-Dodecadienoic acid, 4,6-dimethyl-, (2S,3S)-2-[(1E)-2-carboxyethenyl]-3,6-dihydro-6-oxo-2H-pyran-3-yl ester, (2E,4E,6S)- (9CI) (CA INDEX NAME)

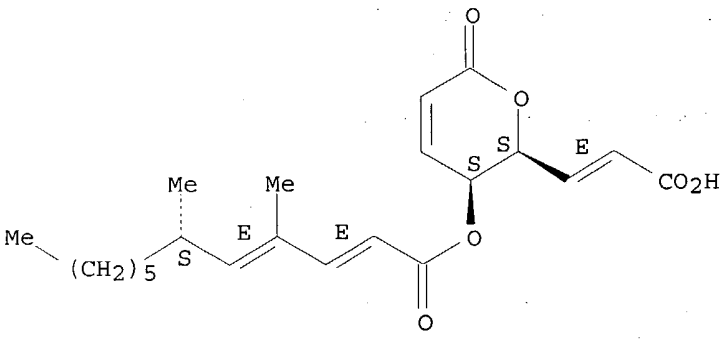
Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:224151 CAPLUS
DOCUMENT NUMBER: 135:32775
TITLE: Scale-up of filamentous organisms from tubes and shake-flasks into stirred vessels
AUTHOR(S): Katzer, Werner; Blackburn, Mark; Charman, Kevin; Martin, Steven; Penn, Julia; Wrigley, Stephen
CORPORATE SOURCE: TerraGen Discovery (UK) Ltd., Slough, UK
SOURCE: Biochemical Engineering Journal (2001), 7(2), 127-134
CODEN: BEJOFV; ISSN: 1369-703X
PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The choice of small-scale fermentation systems contributes significantly to a successful scale-up. Creasing of flasks and the chosen shaker parameters influence the production of secondary metabolites in a strain- and even compound-specific manner. Using actinomycetes and fungi as model organisms the influence of the small-scale fermentation system on the production of various secondary metabolites is described and the effects on screening success and scale-up are considered.
CC 16-2 (Fermentation and Bioindustrial Chemistry)
IT 74720-35-7P, xr334 102228-99-9P, diastovaricin II 157842-16-5P, XR 368 **207220-91-5P**, XR 379 207225-51-2P, XR 573 343780-48-3P
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(scale-up of filamentous organisms from tubes and shake-flasks into stirred vessels)
IT **207220-91-5P**, XR 379
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(scale-up of filamentous organisms from tubes and shake-flasks into stirred vessels)
RN 207220-91-5 CAPLUS
CN 2,4-Dodecadienoic acid, 4,6-dimethyl-, (2S,3S)-2-[(1E)-2-carboxyethenyl]-3,6-dihydro-6-oxo-2H-pyran-3-yl ester, (2E,4E,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

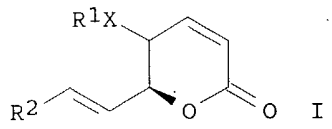


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:720265 CAPLUS
DOCUMENT NUMBER: 131:310551
TITLE: Preparation of dihydropyrones as cytokine production inhibitors.
INVENTOR(S): Hayes, Martin Alistair; Hardick, David James; Tang, Jenny Seukgin; Ryder, Hamish; Folkes, Adrian John; Tatsuoka, Toshio; Matsui, Masashi
PATENT ASSIGNEE(S): Xenova Limited, UK; Suntory Limited
SOURCE: Brit. UK Pat. Appl., 59 pp., 59 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2336362	A1	19991020	GB 1998-8196	19980417
JP 11335365	A2	19991207	JP 1999-109982	19990416
US 6197811	B1	20010306	US 1999-292961	19990416

PRIORITY APPLN. INFO.: GB 1998-8196 A 19980417
OTHER SOURCE(S): MARPAT 131:310551
GI



AB Title compds. [I; X = O, NH; R1 = R3CO, ArCH2, R5OCH2; R3 = R4CH:CH, alkyl, (alkyl-substituted) fluorenyl, oxofluorenyl; R4 = alkyl, alkenyl, aryl, unsatd. heterocyclyl; Ar = aryl; R5 = alkyl optionally interrupted by 1-2 O; R2 = Me, R6O2C; R6 = alkyl], were prepared Thus, di-Et azodicarboxylate in THF was added dropwise to a suspension of phomalactone, Ph3P, and PhCO2H followed by stirring overnight to give 43%

[(2S,3R)-3,6-dihydro-6-oxo-(2E-prop-1-enyl)-2H-pyran-3-yl]benzoate. The latter inhibited IL-1β release from human peripheral blood mononuclear cells with IC50 = 2.4 μM.

IC ICM C07D309-30
ICS A61K031-365

CC 27-13 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT 247188-29-0P 247188-30-3P 247188-31-4P 247188-32-5P 247188-33-6P
247188-34-7P 247188-35-8P 247188-36-9P 247188-37-0P 247188-38-1P
247188-39-2P **247188-40-5P** 247188-41-6P 247188-42-7P
247188-43-8P 247188-44-9P 247188-45-0P 247188-46-1P 247188-47-2P
247188-48-3P 247188-49-4P 247188-50-7P 247188-51-8P 247188-52-9P
247188-53-0P 247188-54-1P 247188-55-2P 247188-56-3P 247188-57-4P
247188-58-5P 247188-59-6P 247188-60-9P 247188-61-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dihydropyrones as cytokine production inhibitors)

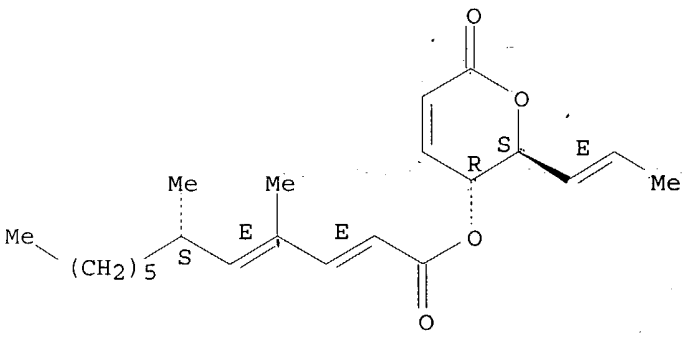
IT 65-85-0, Benzoic acid, reactions 71-23-8, Propanol, reactions 71-36-3, 1-Butanol, reactions 92-92-2, 4-Biphenylcarboxylic acid 98-88-4, Benzoyl chloride 100-39-0, Benzyl bromide 100-52-7, Benzaldehyde, reactions 784-50-9, 9-Fluorenone-2-carboxylic acid 1573-92-8, 9-Fluorenone-1-carboxylic acid 3218-36-8, 4-Biphenylcarboxaldehyde 3970-21-6, 2-Methoxyethoxymethyl chloride 5728-52-9, 4-Biphenylacetic acid 5731-13-5 6276-03-5, 1-Fluorenecarboxylic acid 7071-83-2, 9-Fluorenone-4-carbonyl chloride 14002-51-8, 4-Biphenylcarbonyl chloride 15690-24-1 28921-94-0, Phomalactone 30084-90-3, 2-Fluorenecarboxaldehyde 32466-54-9, trans-2-Dodecenoic acid 73373-17-8, 4-Iodomethylbiphenyl 138875-82-8 **207220-91-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of dihydropyrones as cytokine production inhibitors)

IT **247188-40-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dihydropyrones as cytokine production inhibitors)

RN 247188-40-5 CAPLUS

CN 2,4-Dodecadienoic acid, 4,6-dimethyl-, (2S,3R)-3,6-dihydro-6-oxo-2-(1E)-1-propenyl-2H-pyran-3-yl ester, (2E,4E,6S)- (9CI) (CA INDEX NAME)

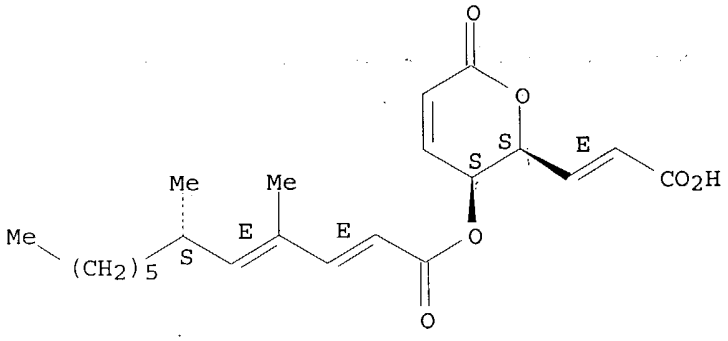
Absolute stereochemistry.
Double bond geometry as shown.



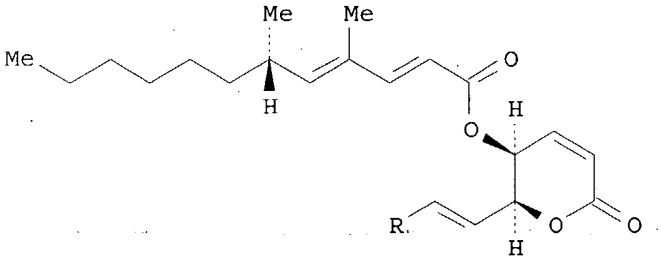
IT **207220-91-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of dihydropyrones as cytokine production inhibitors)

RN 207220-91-5 CAPLUS
CN 2,4-Dodecadienoic acid, 4,6-dimethyl-, (2S,3S)-2-[(1E)-2-carboxyethenyl]-3,6-dihydro-6-oxo-2H-pyran-3-yl ester, (2E,4E,6S)- (9CI) (CA INDEX NAME)

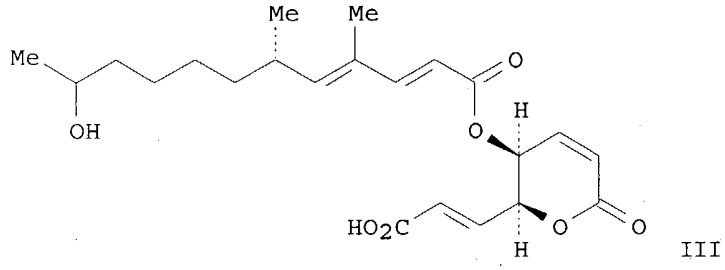
Absolute stereochemistry.
Double bond geometry as shown.



L19 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:709567 CAPLUS
DOCUMENT NUMBER: 132:61362
TITLE: A novel (6S)-4,6-dimethyldodeca-2E,4E-dienoyl ester of phomalactone and related α-pyrone esters from a Phomopsis sp. with cytokine production inhibitory activity
AUTHOR(S): Wrigley, Stephen K.; Sadeghi, Roya; Bahl, Sangeeta; Whiting, Andrew J.; Ainsworth, A. Martyn; Martin, Steven M.; Katzer, Werner; Ford, Robert; Kau, David A.; Robinson, Neil; Hayes, Martin A.; Elcock, Claire; Mander, Thomas; Moore, Michael
CORPORATE SOURCE: TerraGen Discovery (UK) Ltd., Slough, SL1 4EQ, UK
SOURCE: Journal of Antibiotics (1999), 52(10), 862-872
CODEN: JANTAJ; ISSN: 0021-8820
PUBLISHER: Japan Antibiotics Research Association
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I, R=Me
II, R=CO_2H



III

AB A series of novel 6-substituted 5,6-dihydro-5-hydroxy-α-pyrone esters isolated from fermns. of a Phomopsis sp. (Xenova culture collection number X22502) have been identified as inhibitors of lipopolysaccharide (LPS)-induced cytokine production These include the phomalactone (6S)-4,6-dimethyldodecadien-2E,4E-dienoyl ester (I), and two analogs (II and III) bearing a prop-2E-enoic acid moiety at the 6-position of the α-pyrone ring. (6S)-4,6-Dimethyl-2E,4E-dienoic acid and a hydroxylated analog were also isolated and characterized. The most potent cytokine production inhibitor was I, which inhibited LPS-induced tumor necrosis factor α (TNFα) production by U937 cells and LPS-induced interleukin 1β (IL-1β) production by peripheral blood mononuclear cells (PBMC) with IC50 values of 80 nM and 190 nM resp. The effect of I in PBMC was selective for IL-1β relative to TNFα. The inhibition of IL-1β production by I involved a post-translational mechanism of action at the level of IL-1β secretion as demonstrated by the lack of an effect on cell-associated IL-1β production I showed no effect on the activity of caspase 1 in cytosolic exts. from the THP1 monocytic cell line.

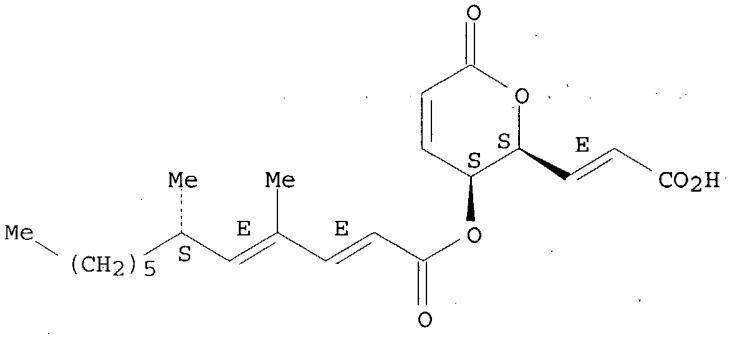
CC 10-1 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 1

IT 138875-82-8P **207220-91-5P 207220-92-6P**
253351-45-0P 253351-46-1P
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(novel phomalactone dimethyldodecadienoyl ester and related pyrone esters from Phomopsis with cytokine production inhibitory activity)

IT **207220-91-5P 207220-92-6P 253351-45-0P**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(novel phomalactone dimethyldodecadienoyl ester and related pyrone esters from Phomopsis with cytokine production inhibitory activity)

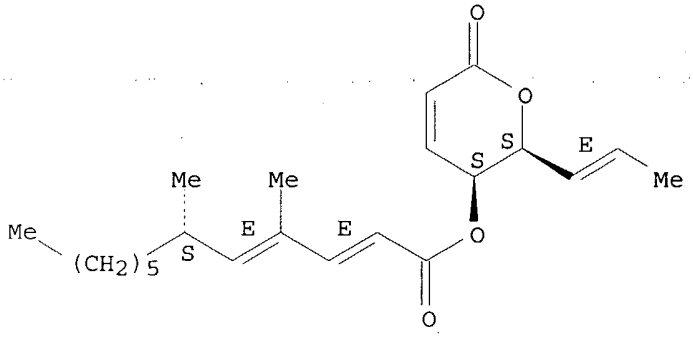
RN 207220-91-5 CAPLUS
CN 2,4-Dodecadienoic acid, 4,6-dimethyl-, (2S,3S)-2-[(1E)-2-carboxyethenyl]-3,6-dihydro-6-oxo-2H-pyran-3-yl ester, (2E,4E,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



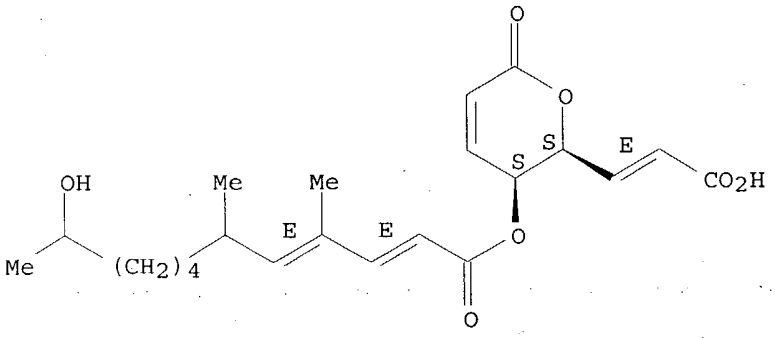
RN 207220-92-6 CAPLUS
CN 2,4-Dodecadienoic acid, 4,6-dimethyl-, (2S,3S)-3,6-dihydro-6-oxo-2-(1E)-1-propenyl-2H-pyran-3-yl ester, (2E,4E,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 253351-45-0 CAPLUS
CN 2,4-Dodecadienoic acid, 11-hydroxy-4,6-dimethyl-, (2S,3S)-2-[(1E)-2-carboxyethenyl]-3,6-dihydro-6-oxo-2H-pyran-3-yl ester, (2E,4E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



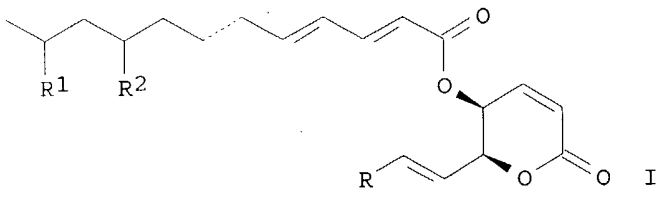
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:268500 CAPLUS
DOCUMENT NUMBER: 128:317258
TITLE: 5,6-Dihydro-α-pyrone cytokine production inhibitors, their production and preparation, and their therapeutic use
INVENTOR(S): Wrigley, Stephen Keith; Bahl, Sangeeta; Guilani, Roya Mansour Sadeghi; Moore, Michael; Katzer, Werner Albert; Martin, Steven Michael; Kau, David Andrew; Whiting, Andrew Jonathan; Robinson, Neil; Hayes, Martin Alistair; Mander, Thomas Haydn
PATENT ASSIGNEE(S): Xenova Ltd., UK; Wrigley, Stephen Keith; Bahl, Sangeeta; Guilani, Roya Mansour Sadeghi; Moore, Michael; Katzer, Werner Albert; Martin, Steven Michael
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9817661	A1	19980430	WO 1997-GB2907	19971021
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9747154	A1	19980515	AU 1997-47154	19971021
GB 2333294	A1	19990721	GB 1999-8624	19971021
GB 2333294	B2	20001018		

PRIORITY APPLN. INFO.: GB 1996-21859 A 19961021
WO 1997-GB2907 W 19971021

GI



AB A 5,6-dihydro-α-pyrone I (R = CO2H or CH3 and R1, R2 = H; or R = CO2H and one of R1 and R2 is H and the other is OH; or when R is CO2H, a pharmaceutically or veterinarily acceptable salt thereof) are provided. Processes for producing these compds., and their use as cytokine production inhibitors, are also described. Fermentative production and preparative esterification are included.

IC ICM C07D309-32
ICS C12P007-40; C12P017-06; C07C059-42; C07C057-03; C12N001-14; C12N001-14; C12R001-645; C12R001-79

CC 1-7 (Pharmacology)
Section cross-reference(s): 16, 27, 63

IT **207220-92-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(5,6-dihydro-α-pyrone cytokine production inhibitors, production and preparation, and therapeutic use)

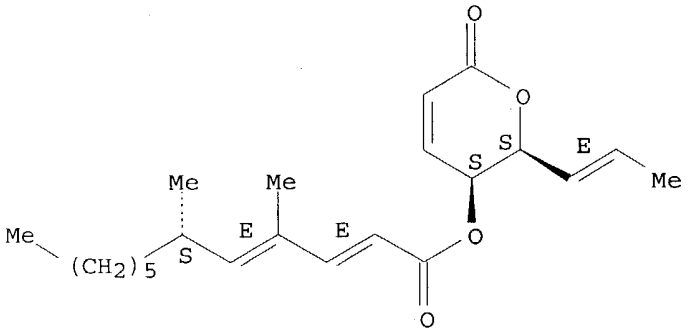
IT **207220-91-5P 207220-93-7P 207220-94-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(5,6-dihydro-α-pyrone cytokine production inhibitors, production and preparation, and therapeutic use)

IT **207220-92-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(5,6-dihydro-α-pyrone cytokine production inhibitors, production and preparation, and therapeutic use)

RN 207220-92-6 CAPLUS

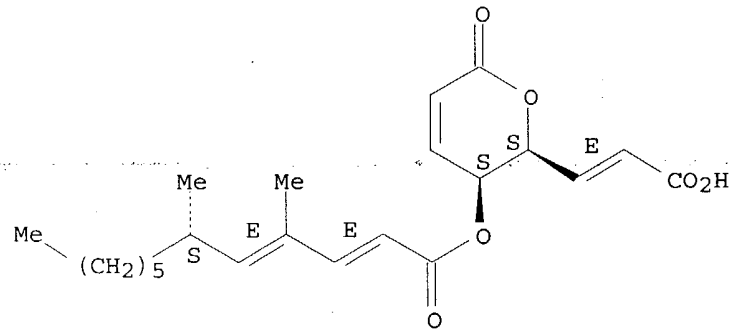
CN 2,4-Dodecadienoic acid, 4,6-dimethyl-, (2S,3S)-3,6-dihydro-6-oxo-2-(1E)-1-propenyl-2H-pyran-3-yl ester, (2E,4E,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



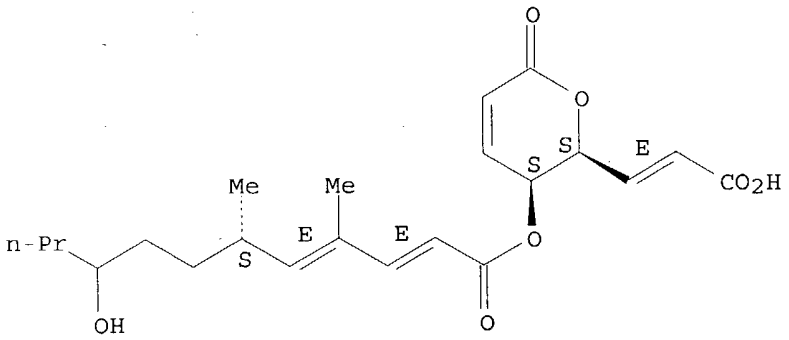
IT **207220-91-5P 207220-93-7P 207220-94-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(5,6-dihydro-α-pyrone cytokine production inhibitors, production and preparation, and therapeutic use)
RN 207220-91-5 CAPLUS
CN 2,4-Dodecadienoic acid, 4,6-dimethyl-, (2S,3S)-2-[(1E)-2-carboxyethenyl]-3,6-dihydro-6-oxo-2H-pyran-3-yl ester, (2E,4E,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



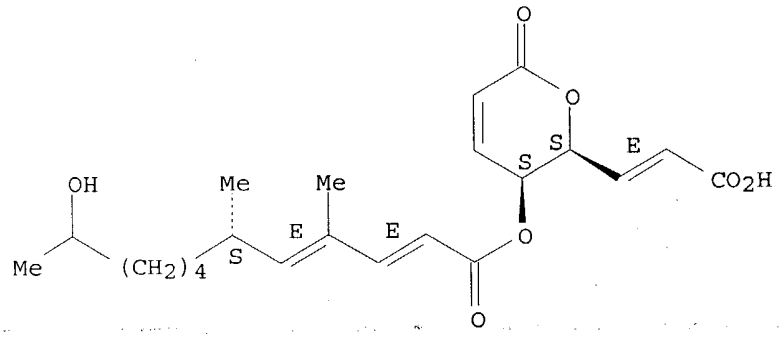
RN 207220-93-7 CAPLUS
CN 2,4-Dodecadienoic acid, 9-hydroxy-4,6-dimethyl-, (2S,3S)-2-[(1E)-2-carboxyethenyl]-3,6-dihydro-6-oxo-2H-pyran-3-yl ester, (2E,4E,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 207220-94-8 CAPLUS
CN 2,4-Dodecadienoic acid, 11-hydroxy-4,6-dimethyl-, (2S,3S)-2-[(1E)-2-carboxyethenyl]-3,6-dihydro-6-oxo-2H-pyran-3-yl ester, (2E,4E,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



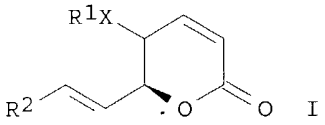
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:720265 CAPLUS
DOCUMENT NUMBER: 131:310551
TITLE: Preparation of dihydropyrones as cytokine production inhibitors.
INVENTOR(S): Hayes, Martin Alistair; Hardick, David James; Tang, Jenny Seukgin; Ryder, Hamish; Folkes, Adrian John; Tatsuoka, Toshio; Matsui, Masashi
PATENT ASSIGNEE(S): Xenova Limited, UK; Suntory Limited
SOURCE: Brit. UK Pat. Appl., 59 pp., 59 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

GB 2336362	A1	19991020	GB 1998-8196	19980417
JP 11335365	A2	19991207	JP 1999-109982	19990416
US 6197811	B1	20010306	US 1999-292961	19990416

PRIORITY APPLN. INFO.: GB 1998-8196 A 19980417
OTHER SOURCE(S): MARPAT 131:310551
GI



I

AB Title compds. [I; X = O, NH; R1 = R3CO, ArCH2, R5OCH2; R3 = R4CH:CH, alkyl, (alkyl-substituted) fluorenyl, oxofluorenyl; R4 = alkyl, alkenyl, aryl, unsatd. heterocyclyl; Ar = aryl; R5 = alkyl optionally interrupted by 1-2 O; R2 = Me, R6O2C; R6 = alkyl], were prepared Thus, di-Et azodicarboxylate in THF was added dropwise to a suspension of phomalactone, Ph3P, and PhCO2H followed by stirring overnight to give 43% [(2S,3R)-3,6-dihydro-6-oxo-(2E-prop-1-enyl)-2H-pyran-3-yl]benzoate. The latter inhibited IL-1β release from human peripheral blood mononuclear cells with IC50 = 2.4 μM.

IC ICM C07D309-30
ICS A61K031-365

CC 27-13 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

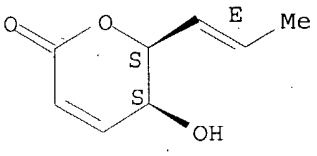
IT 65-85-0, Benzoic acid, reactions 71-23-8, Propanol, reactions 71-36-3, 1-Butanol, reactions 92-92-2, 4-Biphenylcarboxylic acid 98-88-4, Benzoyl chloride 100-39-0, Benzyl bromide 100-52-7, Benzaldehyde, reactions 784-50-9, 9-Fluorenone-2-carboxylic acid 1573-92-8, 9-Fluorenone-1-carboxylic acid 3218-36-8, 4-Biphenylcarboxaldehyde 3970-21-6, 2-Methoxyethoxymethyl chloride 5728-52-9, 4-Biphenylacetic acid 5731-13-5 6276-03-5, 1-Fluorenecarboxylic acid 7071-83-2, 9-Fluorenone-4-carbonyl chloride 14002-51-8, 4-Biphenylcarbonyl chloride 15690-24-1 **28921-94-0**, Phomalactone 30084-90-3, 2-Fluorenecarboxaldehyde 32466-54-9, trans-2-Dodecenoic acid 73373-17-8, 4-Iodomethylbiphenyl **138875-82-8** 207220-91-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of dihydropyrones as cytokine production inhibitors)

IT **107741-12-8P** 247188-62-1P 247188-63-2P 247188-64-3P 247188-65-4P 247188-66-5P 247188-67-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of dihydropyrones as cytokine production inhibitors)

IT **28921-94-0**, Phomalactone **138875-82-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of dihydropyrones as cytokine production inhibitors)

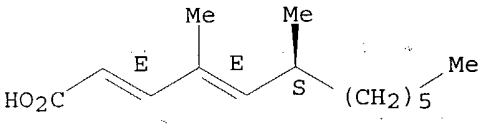
RN 28921-94-0 CAPLUS
CN 2H-Pyran-2-one, 5,6-dihydro-5-hydroxy-6-(1E)-1-propenyl-, (5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



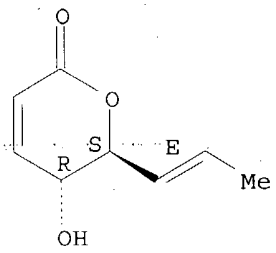
RN 138875-82-8 CAPLUS
CN 2,4-Dodecadienoic acid, 4,6-dimethyl-, (2E,4E,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **107741-12-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of dihydropyrones as cytokine production inhibitors)
RN 107741-12-8 CAPLUS
CN 2H-Pyran-2-one, 5,6-dihydro-5-hydroxy-6-(1E)-1-propenyl-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



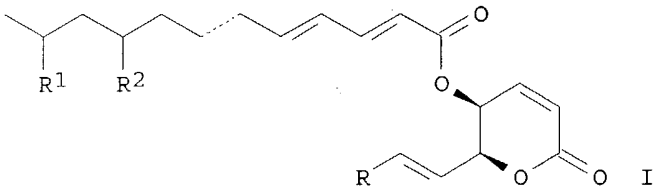
L20 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:268500 CAPLUS
DOCUMENT NUMBER: 128:317258
TITLE: 5,6-Dihydro-α-pyrone cytokine production inhibitors, their production and preparation, and their therapeutic use
INVENTOR(S): Wrigley, Stephen Keith; Bahl, Sangeeta; Guilani, Roya Mansour Sadeghi; Moore, Michael; Katzer, Werner Albert; Martin, Steven Michael; Kau, David Andrew; Whiting, Andrew Jonathan; Robinson, Neil; Hayes, Martin Alistair; Mander, Thomas Haydn
PATENT ASSIGNEE(S): Xenova Ltd., UK; Wrigley, Stephen Keith; Bahl, Sangeeta; Guilani, Roya Mansour Sadeghi; Moore, Michael; Katzer, Werner Albert; Martin, Steven Michael
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9817661	A1	19980430	WO 1997-GB2907	19971021
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9747154	A1	19980515	AU 1997-47154	19971021
GB 2333294	A1	19990721	GB 1999-8624	19971021
GB 2333294	B2	20001018		

PRIORITY APPLN. INFO.: GB 1996-21859 A 19961021
WO 1997-GB2907 W 19971021

GI



I

AB A 5,6-dihydro-α-pyrone I (R = CO2H or CH3 and R1, R2 = H; or R = CO2H and one of R1 and R2 is H and the other is OH; or when R is CO2H, a pharmaceutically or veterinarily acceptable salt thereof) are provided. Processes for producing these compds., and their use as cytokine production inhibitors, are also described. Fermentative production and preparative esterification are included.

IC ICM C07D309-32
ICS C12P007-40; C12P017-06; C07C059-42; C07C057-03; C12N001-14; C12N001-14; C12R001-645; C12R001-79

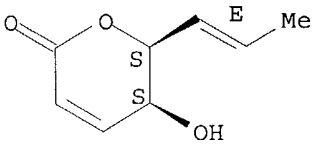
CC 1-7 (Pharmacology)
Section cross-reference(s): 16, 27, 63

IT **28921-94-0P 138875-82-8P 207220-97-1P**
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(reaction; 5,6-dihydro-α-pyrone cytokine production inhibitors, production and preparation, and therapeutic use)

IT **28921-94-0P 138875-82-8P 207220-97-1P**
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(reaction; 5,6-dihydro-α-pyrone cytokine production inhibitors, production and preparation, and therapeutic use)

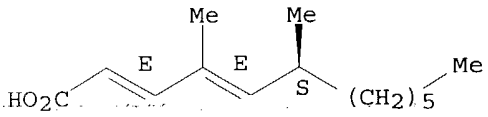
RN 28921-94-0 CAPLUS
CN 2H-Pyran-2-one, 5,6-dihydro-5-hydroxy-6-(1E)-1-propenyl-, (5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



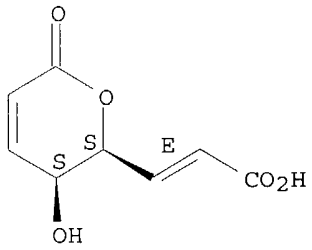
RN 138875-82-8 CAPLUS
CN 2,4-Dodecadienoic acid, 4,6-dimethyl-, (2E,4E,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 207220-97-1 CAPLUS
CN 2-Propenoic acid, 3-[(2S,3S)-3,6-dihydro-3-hydroxy-6-oxo-2H-pyran-2-yl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>